M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

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Date: February 24, 2000

To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: CMC Reviewer Tools

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: CMC Reviewer Tools

Presented for: Trades Meeting

Date Presented: 2/24/200

Presented by: Karen Bernard, Ph.D.

Number of Pages: 13

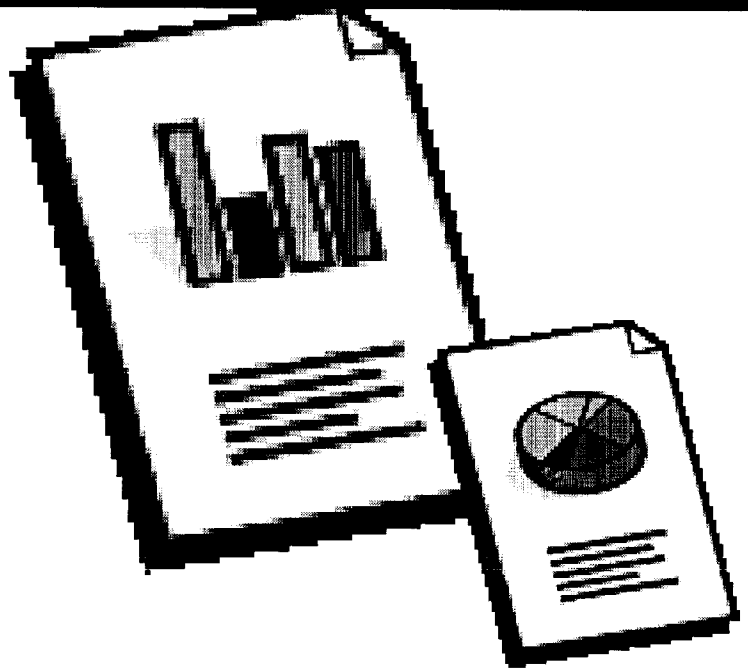
Melissa Lamb

Attachment

90S-0308

M683

CMC Reviewer Tools



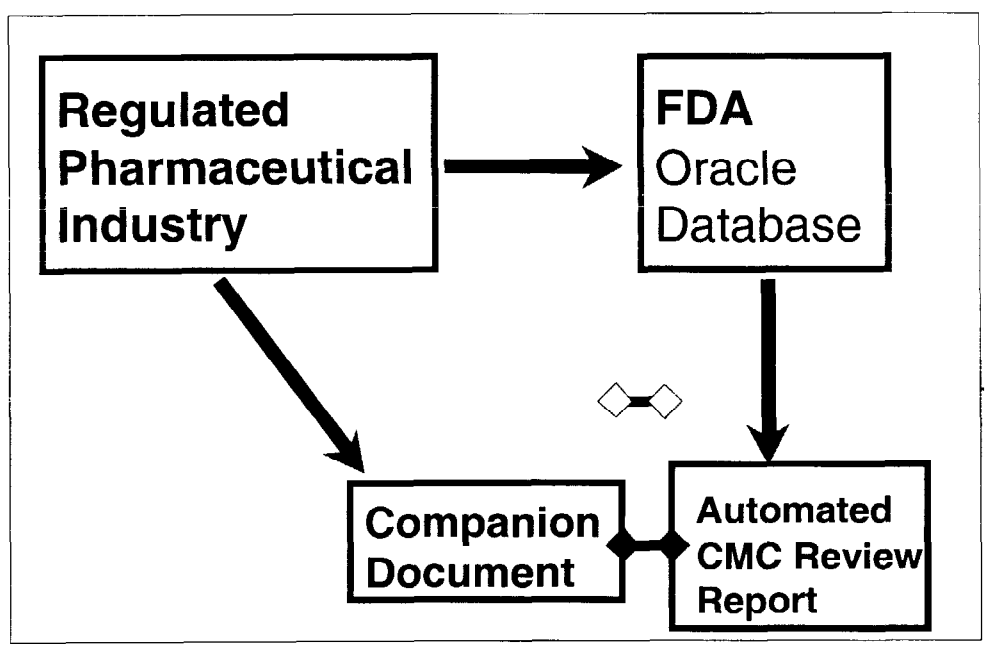
Karen Bernard, Ph.D.

Two Components of CMC Reviewer Tool

- Query OGD database
- Generate CMC review report
  w/ links to Companion Document

Generate CMC Review Report

- **Automatically extract submission data from OGD database into standard 38-point review format**



Companion Document

- Links to major submission sections
- Contain all pertinent review data in an organized fashion
- Copy and paste feature
- References to hard copy kept to a minimum
  (COAs, batch records)

Companion Document

Major CMC Sections for Companion Document

- Components and Composition
- Synthesis - Drug Substance
- Raw Material Controls
- Manufacturing
- Container / Closure
- In-Process Controls
- Finished Product Specifications
- Analytical Method
  - Drug Substance / Drug Product
- Stability

Companion Document

Components and Composition

- Components
  - Quality designation for each component
  - Pharmaceutical use for each ingredient

- Composition
  - Quantitative amount per unit dose and per batch formula
  - Justification for overages

Companion Document

Synthesis

- Cite Type II DMF # referenced, name and address of manufacturer and US Agent

- Reference page of LOA

Companion Document

Raw Material Controls

- New Drug Substance
  - Tabular list of ANDA holder's specifications (Test, limit and method)
  - Lot numbers of COAs from supplier and applicant
  - Purity Profile

Companion Document

Raw Material Controls

- Other Ingredients
  - Tabular list of ingredients and and suppliers
  - Tested per current USP/NF
  - Lot numbers of COAs from supplier and applicant
  - Colors - FDA approved, color certificates
  - Other

Companion Document

Manufacturing

- Description of process, equipment and parameters
- Exhibit Batch (10%)
  - reconciliation data, % yields for each step
  - package entire batch
  - equipment same as Master batch
  - in-process controls
  - holding periods defined
  - process parameters defined
  - deviations filed, preventive action noted
- Master Batch - size defined equipment specified
- Reprocessing Statement

Companion Document

Container / Closure

For each component provide:

- **Manufacturer and DMF reference. LOA**
- **Full description in tabular form**
- **Suitability: compatibility, protection, safety and performance**
- **QC testing (USP and other), COAs, acceptance specifications**
- **Drawings**

Companion Document

Laboratory Controls

In-Process and Finished Dosage Form

- Tabular list of in-process tests, limits and methods
- Tabular list of release specifications
- Methods - USP, validation for non-compendial

  Summary for drug substance and finished product

Companion Document

Stability

- Protocol (Pre and Post Approval)
  - Testing Frequency
    - Long term conditions
    - Accelerated
  - Storage Conditions
    - Long term
    - Accelerated
  - Container Closure
  - Tests and Specifications
- Data
  - Summary of data, specifications
  - Stability indicating methods - stressed
  - Sample data
- Expiration Date